Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
A41530M		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/010558	16.07.2004	16.07.2003
International Patent Classification (IPC) or national classification and IPC		
A61K31/167, A61P17/00, A61P35/00		

Applicant

INSTITUTE OF MEDICINAL MOLECULAR DESIGN. INC.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/010558

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/010558

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	6-16	YES
	Claims	1-5	NO
Inventive step (IS)	Claims		YES
	Claims	1-16	NO
Industrial applicability (IA)	Claims	1-16	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: US 2003/00833386 A1 (J. Yuan), 1 May 2003

Document 2: WO 02/076926 A1 (Schering Corporation), 3 October 2002

Document 3: WO 02/067919 A (SmithKline Beecham Corporation), 6 September 2002

Document 4: JP 11-21225 A (Tanabe Pharmaceutical Co., Ltd.), 26 January 1999

Document 5: WO 02/49632 A1 (Institute of Medicinal Molecular Design, Inc.□, 27 June 2002

Document 6: C. Berking *et al.*, Am. J. Pathol., 2001, 158 (3), pp. 943-953

Document 7: R. K. Singh *et al.*, Histol. Histopathol, 2000, 15, 843-849

Claims 1-5

Document 1 (claim 6 and fig. 3) and document 2 (claim 35 and examples 34-37 and 40) disclose the fact that compounds falling within the scope of compounds represented by general formula (I) in the description of the present application can be used for treating melanoma.

Document 3 (page 1, lines 20-26, and Biological Examples) discloses the fact that compounds falling

within the scope of compounds represented by general formula (I) in the description of the present application inhibit receptor binding of Gro-α, which has melanoma growth stimulating activity.

Document 4 (Example 1) discloses the fact that compounds falling within the scope of compounds represented by general formula (I) in the description of the present application suppress melanin production.

Therefore, the inventions set forth in claims 1-5 are not novel and do not involve an inventive step in the light of documents 1-4.

Claims 1-16

Document 5 (claim 13) discloses compounds falling within the scope of compounds represented by general formula (I) in the description of the present application which suppress expression of TNF-α, IL-1 and IL-8; and the inventions set forth in claims 1-16 differ from the aforementioned disclosure in the use of said compounds for preventing and/or treating pigment deposition and/or skin cancer.

However, document 6 (page 943, right column, lines 4-3) and document 7 (page 845, left column, lines 38-47) disclose the fact that expression of TNF-α, IL-1 and IL-8 causes melanoma growth, development and transformation.

Therefore, a person skilled in the art could easily use compounds falling within the scope of compounds represented by general formula (I) in the description of the present application disclosed in document 5 to prevent and/or treat melanoma, which is a skin cancer, by

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

suppressing expression of TNF-α, IL-1 and IL-8, to give the inventions set forth in claims 1-16.

Therefore, the inventions set forth in claims 1-16 do not involve an inventive step in the light of documents 5-7.

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Box No. VI **Certain documents cited**

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 03/103655A1 [EX]	18.12.2003	05.06.2003	10.06.2002
WO 2004/006906 A2	22.01.2004	15.07.2003	15.07.2005
[EX]			02.08.2002
			03.04.2003

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)

Box No. VIII **Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-9 and 11-16

Claims 1-9 and 11-16 relate to medicaments which contain a compound represented by formula (I) in claim 1 as an active ingredient.

However, the chemical structure shared by compounds represented by formula (I) is a very small part of the entire structure of the compounds, and since it embraces a large number of sets of compounds which are imprecise to the extent of not being able to specify the specific compounds comprehended therein and are very different from one another in chemical structure, and from the description a melanocyte growth suppression test was only confirmed on one compound, it cannot be recognized from said account in the description that other compounds represented by formula (I) all have the same action as the tested compound.

Therefore, it is deemed that other than as they relate to the invention set forth in claim 10 and equivalent compounds, which can be recognized to have a chemical structure equivalent to the compound which is confirmed within the description to have the specified action, these inventions are not clearly and fully supported by the claims and the description to the extent that a person skilled in the art can carry out the inventions.

In addition, the compounds which are specific active ingredients in claims 14 and 15 are described using specification by means of document numbers; however, it is completely impossible, on the basis of these claims

Box No. VIII Certain observations on the international application

and the description to judge the nature of the compounds which fall within the scope thereof. Therefore, the inventions set forth in these claims cannot be said to be clearly and concisely defined by the aforementioned description. This also applies to claim 16, which refers back to these claims.

Since the present application is thus not fully disclosed, an international preliminary examination report has been prepared with reference to disclosures within a logical scope given the scope of the inventions disclosed in the description.